

R E M A R K S

Rebuttal of Examiner's Comments in Advisory Action

Within the comments of the Advisory Action, the Examiner cites *Ex parte Quadranti* as proper basis for maintaining the outstanding obviousness rejection. 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992). However, it is Applicants' position that the Examiner is misapplying *Quadranti*.

First, *Quadranti* states that the statistical significance of the results must be considered and that the methods of demonstrating synergism are many. 25 USPQ2d 1073. The Examiner appears to have taken the position that the results provided by Applicants are not "statistically significant." However, as to the question of statistical significance, "it would seem that art-recognized tests as carried out by trained scientists and incorporated into a patent application should be believed by the Patent and Trademark Office in the absence. . . of any evidence to *doubt* the correctness of the test results or their statistical significance. (Emphasis in original)" *In re Kollman and Irwin*, 201 USPQ 193 (CCPA 1979) (finding that in herbicide cases, unobviousness of a broader claimed range can be proven by a narrower range of data).

The Examiner has not set forth any evidence to doubt the correctness of the test results or their statistical significance. *Quadranti* does not summarily dismiss the Colby equation as an appropriate measure of synergy, as the Examiner attempts to suggest. On the contrary, in *Quadranti*, the Examiner "indicated certain clear anomalies that the Colby equation gives rise to." Thus, the Colby equation was found inappropriate in that limited, case-specific instance. Here, there is no evidence of record that the results presented by Applicants, derived from the Colby equation, should not be taken at face value as "statistically significant." Moreover, in light of *Kollman*, Applicants' results should be presumed to be statistically significant.

Second, *Quadranti* and *Ex parte The NutraSweet Co.*, 19 USPQ2d 1586 (Bd. Pat. App. & Int. 1991), establish that differences of practical advantage in combination with arguments of

statistical significance can rebut an obviousness rejection. Here, Applicants have shown that the presently claimed invention yields unexpectedly synergistic results. Moreover, the presently claimed invention possesses the practical advantage of being particularly suitable for controlling powdery mildew fungi (see specification of present invention at page 3, lines 16-20 and page 8, lines 11-30). Therefore, Applicants submit that the results and arguments presented herein are sufficient to overcome the outstanding obviousness rejections.

Issues under 35 U.S.C. 103(a)

Claims 1-10 have been rejected under 35 USC §103(a) as being unpatentable over Muller '684 (Canada Patent No. 2,434,684) and Wakai '028 (EP 1 077 028).¹ Basically, it is the position of the Patent Examiner that Muller '684 discloses combinations including all of components (2)-(4), Wakai '028 discloses fungicidal mixtures including component (1), and it would have been obvious to one skilled in this technological area to combine the mixtures of Muller '684 with Wakai '028 in order to obtain the mixtures claimed in the present application. This rejection is traversed based on the following reasons.

Present Invention and Its Advantages

The present invention is directed to synergistic fungicidal mixtures which include: a benzamideoxime compound of Formula (I) as component (1); a benzophenone of Formula (II) as component (2); epoxiconazole of Formula III as component (3); and, optionally, pyraclostrobin of Formula IV as component (4). As the comparative test results in Table 6 at pages 16-17 of the specification indicate, the combination of at least components (1)-(3) exhibits an advantageously and unexpectedly improved fungicidal efficacy over both the single components applied separately (Table 2) and the different sub-combinations of two components in Tables 3-5. Additional comparative test results supporting the patentability of the claims of the present application are presented in Tables 7-11. See Discussion of Data in Specification, detailed below.

¹ Claims 1-14 were actually pending in the present application at the time the previous Office Action was mailed. New claims 11-14 were filed in the response dated October 12, 2006. It is presumed that the Examiner inadvertently left out claims 11-14.

Distinctions Over Cited References

Muller '684 discloses a synergistic mixture of three components including a benzophenone (I), a carbonate (II) and an azole (III), which correspond to present components (2), (3) and (4), respectively.

Muller '684 does not teach the combination of the compounds as presently claimed. Muller '684 fails to disclose or suggest the use of the benzamideoxime compound as employed in component (1) of the composition of the present invention. Further, Muller '684 fails to provide any hint or suggestion that such a benzamideoxime compound be used in described composition. Thus, significant patentable distinctions exist between the present invention and Muller '684.

Wakai '028 discloses mixtures, which include various benzamideoxime compounds which may be used in mixtures with a variety of other compounds as noted, for example, at paragraphs [0002] – [0003]. However, the benzamideoxime compounds of Wakai '028 do not correspond to present component (1).

Not all biological examples are prepared with compound no. 1 in Table 1 of Wakai '028. Moreover, this compound no. 1 has a substituent CF_3 for X^1 , whereas compound (I) of the present invention has a OCF_2 substituent in this position. This means that in the Wakai '028 reference, no compound (I) of component (1) of the present invention has been tested.

Wakai '028 also fails to disclose or suggest the use of either of components (2) or (3) as employed in the composition of the present invention. Wakai '028 also fails to disclose or suggest the use of component (4) which is employed in some of the embodiments of the present invention. Thus, significant patentable distinctions exist between the present invention and Wakai '028.

The Examiner concludes that the claimed invention would have been obvious from the teaching of the cited prior art in the absence of any criticality and/or unexpected results. However, the finding of synergy is always an unexpected result, because it is in principle not predictable.

It is further submitted that there fails to be a basis for a motivation to one skilled in the art to take a benzamideoxime compound from Wakai '028 and combine this with at least a specific compound corresponding to component (2) and another specific compound corresponding to component (3) described in Muller '684. At best, the disclosures of Muller '684 and Wakai '028 provide a general suggestion for experimentation involving a vast multitude of combinations, without any specific suggestion that the combination of components (1) – (3) employed in the present invention will provide synergistic fungicidal results. Thus, there fails to be an adequate basis for combining Muller '684 with Wakai '028, other than improper "hindsight reconstruction" based on the disclosure of the present application.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Since the combination of Muller '684 and Wakai '028 does not teach or suggest all the limitations of the presently claimed invention and does not provide any suggestion for arriving at the claimed synergistic fungicidal mixture, Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness and request that the above-noted rejection under 35 U.S.C. §103(a) be withdrawn.

Even assuming hypothetically that *prima facie* obviousness has been properly alleged, such obviousness is rebutted by the evidence of advantageous, unexpected properties discussed below in connection with the comparative test evidence provided in the present specification.

Discussion of Data in the Specification

Applicants direct the Examiner's attention to attached **Exhibit A**. Exhibit A includes reproductions of Tables 2-6, from the present specification. Here, the biological results of "use Example 1" are disclosed, which is the fungicidal activity against mildew of wheat. For the Examiner's convenience, Applicants have added, on the right side of the Tables, the degree of synergy in percentage, which is the difference between the calculated efficacy and the observed efficacy. The bigger the difference is, the higher the degree of synergy.

In order to adequately evaluate the results, Applicants have compared the results Tables 3 and 4 with the results of the first 8 biological results of Table 6, because in Table 3 the results of the mixtures of metrafenone + epoxiconazole are listed and in Table 4 the results of compound I + metrefenone are listed. The first biological results of Table 6 are based on the mixtures of compound I + metrafenone + epoxiconazole.

Additionally, Applicants have compared the results of Table 5 with the results of the second 8 biological results of Table 6, because in Table 5 the results of the mixtures of metrafenone + pyraclostrobin are disclosed. The second 8 biological results of Table 6 are based on the mixtures of compound I + metrafenone + pyraclostrobin.

Two major differences could be observed:

1. The observed efficacy of 12 mixtures in Table 6 are higher than 90%, 8 mixtures are higher than 95%, 3 mixtures are 100%. Only 4 mixtures are below 90%, which are 87%, 78%, 83% and 83%.

The observed efficacy of the 12 mixtures in Tables 3, 4, and 5 are all below 90%, 10 mixtures are below 80% and 3 mixtures are below 70%.

These results clearly demonstrate a higher efficacy of the inventive mixtures versus the mixtures of the prior art. This is an unexpected result.

2. The degree of synergy in percentage (%) of the difference of calculated efficacy and the observed efficacy is in general higher for the inventive mixtures. The degree of synergy for the mixtures in Table 6 is for 14 mixtures 9% or higher, with the exception of 2 mixtures, which are below 9%.

The degree of synergy for the mixtures in Tables 3-5 is for 7 mixtures, 9% or below, and for 5 mixtures above 9%.

These results also clearly show in general a higher degree of synergy for the inventive mixtures, which is unexpected and unpredictable.

Similar results can be derived from the data of the use Example 2, disclosed in Tables 7-11 with the major difference being that the data of the mixtures of the prior art (disclosed in Table 9) show no efficacy at all.

Therefore, it follows, that the data in the specification clearly support unexpected results in form of a higher efficacy and higher synergy of the mixtures of the present invention in comparison to the mixtures of the prior art. Consequently, the synergistic fungicidal mixture of the present invention is unexpected and unobvious.

Conclusion

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Monique T. Cole, Reg. No. 60,154

at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

Dated:

JUN 5 2007

Respectfully submitted,

By _____

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Attachment: **Exhibit A**